REMARKS

Reconsideration and allowance are respectfully requested.

Claims 3-8, 10, 12, 15-17, 25, 35-53, 55 and 57-63 are pending. Upon an indication that a product claim is allowable, rejoinder of process claims is requested.

Specification

Applicants thank the Examiner for pointing out informalities in the specification. As suggested by the Examiner, the typographical error on page 5 is corrected and the word "etc" is deleted by the present amendment.

Withdrawal of the objection is requested.

35 U.S.C. 112 – Definiteness

Claim 17 was rejected under Section 112, second paragraph, as being allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Applicants traverse because the present amendment (deletion of the word "assay") is believed to moot the rejection.

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

35 U.S.C. 112 – Written Description

The specification must convey with reasonable clarity to persons skilled in the art that applicant was in possession of the claimed invention as of the filing date sought. See *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). But the Patent Office has the initial burden of presenting evidence or a reason why persons of ordinary skill in the art would not have recognized such a description of the claimed invention in the original disclosure. See *In re Gosteli*, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

Claims 3-4 and 17 were rejected under Section 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants traverse.

The Examiner alleges on page 4 of the Action that "[t]he specification does not clearly describe the derivatives of ubiquitin, or the fragments or derivatives of a protein."

Applicants urge that claims 3, 4 and 17 are clear in view of their disclosure in the specification. The specification states, "A person of ordinary skill in the art will recognize that the present invention relates not only to the specific protein sequences disclosed in the specification, but also to protein variants thereof such as fragments, analogs and/or derivatives." (Specification, page 42). The specification further provides examples of what Applicants regard as protein fragments and variants. (See specification, pages 41-42 and 43-45 respectively).

For example, the specification describes, "The present invention includes protein sequences that are at least 60% . . . similar or identical to an amino acid sequence selected from a group listed in Table 1." (Specification, page 44). It also describes, "Still within the scope of the invention are preferred segments of interest of the sequences of the present invention which are comprised of at least 10 . . . amino acid residues." (Specification, page 44). It further describes, "The proteins of the invention can be post-translationally modified. . . . The proteins of the invention may include unnatural amino acids formed by post-translational modification or by introducing unnatural amino acids during translation." (Specification, page 44).

Consequently, a skilled artisan would readily recognize what Applicants regard as their invention.

Although Applicants disagree with the basis of the Examiner's rejection, in order to further the prosecution and more clearly define the technical features of the present invention, claims 3 and 17 are amended by clearly reciting that fragments or derivatives comprise "polypeptides of at least 10 amino acids having at least 60% sequence similarity to their respective protein." Claim 4 is dependent on claim 3.

Withdrawal of the written description rejection made under Section 112, first paragraph, is requested because the specification conveys to a person skilled in the art that Applicants were in possession of the claimed invention as of the filing date.

35 U.S.C. 102 – Novelty

A claim is anticipated only if each and every limitation as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal*

Bros. v. Union Oil Co. of Calif., 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is claimed. See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Claims 3-4 and 17 were rejected under Section 102(b) as allegedly anticipated by Maeda et al. (FEBS Lett. 494:181-185, 2001). Applicants traverse.

The elected claims recite that the complex is formed via N-end rule ubiquitylation. (See claims 3, 17, 57 and 59). Contrary to Applicants' disclosure in the specification, Maeda et al. teach autoubiquitylation of cullin by a non N-end rule pathway. The fact that Maeda et al. use an N-terminal myc-cullin fusion and detect the product by binding to the N-terminal myc sequence is a clear indication that the substrate did not contain a destabilizing N-terminal residue (as required for N-end rule ubiquitylation) and that the substrate was not processed to expose a destabilizing N-terminal residue. (See Maeda et al., page 184). Therefore, Maeda et al. do not teach the claimed subject matter.

Claims 3-4 and 17 were rejected under Section 102(b) as allegedly anticipated by Elsasser et al. (Mol. Biol. Cell 10:3263-3277, 1999). Applicants traverse.

Elsasser et al. disclose five deletion mutations (Δ8-46, Δ3-16, Δ13-26, Δ23-36 and Δ33-46). (Elsasser et al., page 3269, Figure 2). All of these mutations preserve the N-terminal amino acid which is not a destabilizing N-terminal residue as required for N-end rule ubiquitylation. (See specification, page 4). Furthermore, the reference shows that under the conditions used by Elsasser et al., ubiquitylation does not occur through the N-end rule pathway. This result was demonstrated by the requirement observed by Elsasser et al. that ubiquitylation required phosphorylation of Cdc6. Therefore, Elsasser et al. do not teach the claimed subject matter.

Claims 3-4 and 17 were rejected under Section 102(b) as allegedly anticipated by Morishima-Kawashima et al. (Neuron 10:1151-1160, 1993). Applicants traverse.

Ubiquitylation by the N-end rule pathway occurs through the recognition of type I or type II destabilizing N-terminal residues. Type I residues are Arg, Lys and His; type II residues are Phe, Leu, Trp, Tyr and Ile. (Specification, page 4). In contrast, Morishima-Kawashima et al. specifically teach that out of six ubiquitylated sequences, four start with glutamic acid (Glu, E), one starts with valine (Val, V) and one starts with serine

(Ser, S). (Morishima-Kawashima et al., page 1155, Table 1). None of these amino acid residues is a destabilizing N-terminal residue required for N-end rule ubiquitylation. (See specification, page 4). Consequently, Morishima-Kawashima et al. do not teach the claimed subject matter.

Withdrawal of the Section 102 rejections is requested because all limitations of the claimed invention are not disclosed by the cited references.

Conclusion

Having fully responded to all of the pending objections and rejections contained in this Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

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